SARCOIDOSIS OF THE TESTIS: A CASE REPORT

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A left testicular mass was found in a 34-year-old black man with a history of multisystem sarcoidosis of 7½ years duration. Microscopic examination of the excised testicle revealed noncaseating granulomas throughout, as well as a few such lesions in the epididymis. This is the seventh reported, microscopically proven case of sarcoidosis of the testis without significant epididymal involvement occurring in a living individual.

A review of the other cases of testicular sarcoidosis in the literature reveals that most of them had a number of organs involved with this disease, similar to the subject of this report. Over one half of these patients had skin lesions with or without bone or joint manifestations, suggesting that the testis should be evaluated with particular care when any of these areas are involved. If there is a consistent association of skin, bone, and testicular lesions in this disease, genital sarcoidosis may be more common than presently thought.

The testis is one of the rarest organs to be infiltrated with sarcoidosis granulomas. To date, 12 such cases have been reported.[1-12] Only seven have been described in living individuals.[6-12] All of these patients had testicular biopsies except one; he was considered to have sarcoidosis of this organ because of a testicular mass and multiple lesions elsewhere in the body.[2] Thus, six biopsy proven cases of sarcoidosis of the testis in living patients have been reported.[7-12] A recent patient with sarcoidosis studied at Howard University Hospital was found to have a testicular mass in which noncaseating granulomas were found. This represents the seventh reported case of sarcoidosis of testis pathologically proven antemortem without significant epididymal involvement and is the subject of this report.

CASE REPORT

K.L., a 34-year-old black man, was admitted to Howard University Hospital in March 1983 because of a painless left testicular mass. Sarcoidosis had been diagnosed by a mediastinal node biopsy in October 1975. He was hospitalized because of dyspnea; a chest x-ray film showed bilateral hilar lymphadenopathy and diffuse, interstitial nodular lesions throughout both lung fields. Physical examination on the first admission revealed that his penis and both testicles were slightly smaller than normal for an individual who was 76 inches tall and weighed 197 pounds. No medication was prescribed because pulmonary function was only slightly diminished.

About nine months later, in 1976, he developed diffuse, cystic subcutaneous nodules of the left hand, arm, and epitrochlear area; a biopsy revealed noncaseating granulomas. A few days later he noticed cervical lymphadenopathy and enlargement of both parotid glands, and x-ray films of the hands showed cystic bone lesions. Prednisone was started and there was rapid regression of the size of the enlarged lymph nodes, parotid glands, and the subcutaneous nodules. Therapy was continued for one year during which time he

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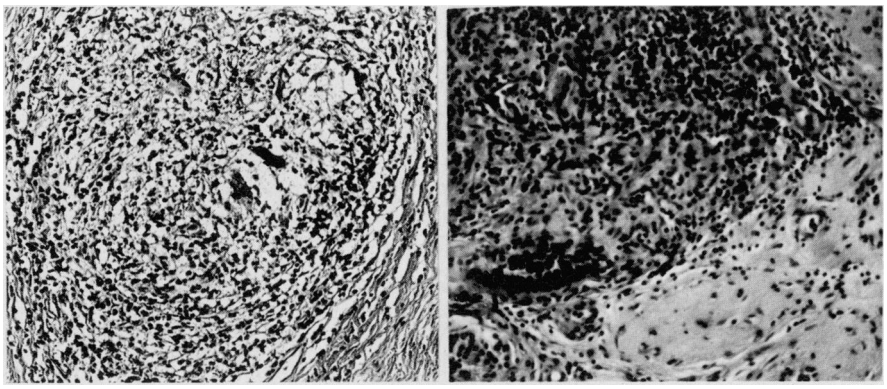

Figure 1. Photomicrograph of the testis showing a noncaseating granuloma. Note epithelioid and multinucleated giant cells (left). Hyalinized seminiferous tubules are noted adjacent to a granuloma (right)

was asymptomatic; however, when he stopped the prednisone, cervical lymphadenopathy reappeared within a few weeks. Again, the node enlargement disappeared with steroid treatment.

Nine months later (in early 1978), he noticed nasal swelling and flat hypopigmented lesions of the butterfly area of the face. Several weeks earlier, he had stopped taking the prednisone. Noncaseating granuloma was present in a biopsy specimen of the nasal mucosa. At the same time, there was also cervical lymphadenopathy; prednisone (30 mg daily) was given for one month and a decrease in the nasal swelling and node enlargement occurred. The skin lesions almost disappeared during the same period of time.

For the next three years, he was well except for recurrent episodes of severe nasal congestion, which corresponded with discontinuance of the prednisone. His nasal congestion improved greatly when steroid therapy was reinstituted, but recurred each time he stopped the drug. During that time, there was also steady weight gain of almost 50 pounds yearly. By August 1981, he weighed 347 pounds, 150 pounds more than he did on his first admission. For about one year he also had marked polydipsia and polyuria for which he was hospitalized. He was discharged with the diagnoses of iatrogenic Cushing's disease, hypogonadism, and psychogenic polydipsia as well as multisystem sarcoidosis. The prednisone dosage was decreased, and he lost weight steadily for about six months. He was lost to follow up for the subsequent 18 months.

When next seen in February 1983, he had lost 107 pounds and admitted progressive change in the contour of his nose. He was readmitted to the hospital and found to have recurrence of the skin lesions in the butterfly area of the face, collapse of the nasal bone, a 3×2 cm mass of the left testicle, and a very small right testicle. A gallium scan revealed increased uptake in the parotid glands, nose, and the lungs, consistent with sarcoidosis. Prednisone was restarted, and the patient was discharged to be followed by the urologic service.

In March 1983, he was admitted to urology for study of the left testicular mass. Physical examination revealed the following: temperature 98.6° F, pulse 80 beats/min, and blood pressure 136/84 mmHg. His face was puffy, and the skin revealed multiple hyperpigmented areas on the left arm, back, and both legs. A hypopigmented macular rash was present over the "butterfly" area of the face. A healed surgical scar was present in the suprasternal notch and a keloid over the midsternal area. These resulted from the mediastinoscopy and sternal marrow biopsy, both of which had been performed during earlier hospitalizations. Purple striae were seen on the abdomen. The neck was normal without lymphadenopathy. The heart size was normal; no murmurs or gallops were present and the rhythm was regular. A few fine rales were present at the base of both lungs; the abdomen revealed no masses, organomegaly, or tender areas. The penis was quite small for a man of the patient's size; the right testis was very small, but the left testis was enlarged, measuring 7×4 cm with a 3×2 cm mass; it was firm, but not tender or fluctuant. The remainder of the examination was normal.

The laboratory studies were all normal, including the following: the complete blood count and differential, urinalysis, serum sodium, chloride,

TABLE 1. FEATURES OF BIOPSY PROVEN TESTICULAR SARCOIDOSIS

Author	Date	Chest X-Ray Film	Extrapulmonary Lesions
Krause[7]	1958	BHL*	Subcutaneous nodules on left arm and both thighs. Hand X-ray films of cysts on distal phalanx of left 5th finger
Chowdhury[8]	1973	BHL DIG**	Enlarged right lacrimal gland: skin lesions. Hand X-ray films of destruction of the phalanges third finger and thumb of the right hand
Opal et al[9]	1979	BHL	Swelling and tenderness of the right knee
Torrington et al[10]	1979	BHL	
Wees et al[11]	1981	BHL	Tender and swollen left knee and ankle. Papulosquamous skin lesions and generalized lymphadenopathy
Seaworth et al[12]	1983	BHL	
Hackney, Jackson*** and Worrell	1984	BHL DIG + fibrosis	Skin with hypopigmented lesions of the face; hyperpigmented lesions left arm, both legs, and back. Cervical lymphadenopathy. Bilateral parotid enlargement. Nasal bone destruction. Cystic Hands

*BHL—Bilateral hilar lymphadenopathy
**DIG—Diffuse interstitial granulomas
***The case reported herein

total protein and albumin/globulin ratio, blood urea nitrogen, cholesterol, calcium, bilirubin, alkaline phosphatase, lactic acid dehydrogenase, uric acid, glucose, inorganic phosphorus, serum glutamic pyruvic transaminase and potassium. A test for venereal disease was nonreactive.

A left orchiectomy was performed; on examination, the testicle was enlarged and measured $6 \times 5.5 \times 3$ cm. It was surrounded by white fibrous tissue and imparted a brownish-tan color on cut surface.

On light microscopy, the testis and epididymis showed noncaseating granulomas consisting of sharply delimited collections of epithelioid cells, among which were occasional multi-nucleated giant cells. At the periphery, small zones of lymphocytes and plasma cells were seen. Special stains for acid-fast bacilli and fungi were negative.

There was extensive fibrosis. Many of the seminiferous tubules showed thickened, tubular-basement membranes lined with degenerated spermatogonia and sertoli cells. The seminiferous tubules were generally small and widely separated. Many were completely atrophic and replaced by hyalinized masses. Hyperplasia of the interstitial cells of Leydig was not evident (Fig 1).

DISCUSSION

This patient had sarcoidosis involvement of a number of organs throughout the body including the parotid glands, the nasal bone and mucosa, cervical and hilar lymph nodes, bones of the fingers, and the lungs. The testicular lesion did not become apparent until almost $7\frac{1}{2}$ years after the initial diagnosis of sarcoidosis. His differs from other reported cases listed in Table 1 in that the testicle was involved at the initial recognition of the disease. From Table 1, it can be seen that this

patient resembles the other cases in every other respect, as all of them had multisystem disease. Complete physical examinations were described in four of the six patients listed in Table 1; skin or subcutaneous lesions were present in three of the four, not unusual as about one of 11 patients with sarcoidosis have such involvement.[13] Two patients had joint signs and symptoms, which are quite unusual. In his review of sarcoidosis arthritis in 1963, Kaplan[14] cited only 95 well-documented cases, and James[13] et al do not mention joints in their survey of over 3,600 cases of sarcoidosis in patients living in 11 cities throughout the world. This suggests that the scrotum should be examined especially carefully, if a sarcoidosis patient presents with arthritic complaints or skin lesions.

As Table 1 shows, three of the patients described had lesions of the bone; two had destructive lesions. One of them had a destroyed phalanx of the third finger of the left hand; the other (the subject of this report) had destruction of the nasal bone. Finding bone lesions in three of seven sarcoidosis patients is distinctly unique, as James et al[13] found osseous abnormalities in only 3 percent of the cases in their survey. At Howard University Hospital, bone lesions were present in seven of 50 patients (14 percent).[15] It may be speculated that testicular involvement in sarcoidosis is probably much more common than the literature suggests, if testicular lesions are as frequent when bone sarcoidosis is present. By this reasoning, three-sevenths of sarcoidosis-afflicted men with bone lesions would be expected to have involvement of the testis. From the experience of James' group,[13] testicular lesions should be found in 1.3 percent of men with sarcoidosis (ie, $^3/_7 \times 3$ percent). On the other hand, the Howard University Hospital experience[15] indicates that testicular sarcoidosis should be found in 6 percent of all men with the disease (ie, $^3/_7 \times 14$ percent).

The patient reported here had a very small right testis as well as significant fibrosis of the involved left testis. As the right testis was not examined microscopically, it is not known whether its decreased size was due to atrophy or contraction secondary to fibrosis, ie, healing of noncaseating granulomas. Pulmonary fibrosis commonly occurs when the noncaseating granulomas of sarcoidosis of the lung heal. Thus, it is reasonable to assume that fibrosis may result from the healing of testicular granulomas and the testis may present either as a firm smaller-than-normal organ, or as a mass as described in this case and in the cases listed in Table 1. To the authors' knowledge, a prospective study of testicular abnormalities in sarcoidosis has not been done; a plan for such an investigation is in progress. One feature of the new study will be to determine (by physical examination) whether the testis is more often involved than generally recognized, and whether shrinking of the organ occurs with significant frequency in these patients.

How is testicular function affected by sarcoidosis of the testis? The patient reported here had evidenced diminished function by a small penis, small right testicle, and a serum testosterone of less than 20 ng/dL (normal 300 to 1200 ng/dL). Of the cases listed in Table 1, only the patient reported by Opal et al[9] had a testosterone level measured; it was normal, but hypothalamic function was diminished. No statement was made as to whether there was sarcoidosis of the hypothalamus. Only this case study patient was reported to be eunuchoid, but he did not undergo a complete study of his testicular function, and he claimed to have no children. No information was available about the sexual habits, parentage, or the martial status of the patients listed in the Table; thus, no definitive statement can be made about the effect of testicular sarcoidosis on sexual function. The determination of testicular function in men with sarcoidosis will be one of the aims of the authors' projected study of these organs in this disease.

CONCLUSIONS

When a testicular mass is found in any patient, it is important to determine whether a tumor is present. This is a difficult question to answer when the patient is black and has sarcoidosis, as testicular tumors are rare in this race. Only six other cases of sarcoidosis of testis have been reported. Daniels et al[16] reported that of 850 testicular tumors found in several surveys, only 16 occurred in blacks. In the populations surveyed, blacks accounted for 12 to 30 percent of the total. During the 11-year period from 1972 to 1983, four germ cell tumors and two gonadal stromal tumors were found by the Urology services[7,18] at the District of Columbia General and Howard University Hospitals. The patients at these facilities are virtually all black.

Testicular sarcoidosis should be suspected when features of this disease exist elsewhere, eg,

chest x-ray films with typical lung lesions, especially when bilateral hilar lymphadenopathy is present. Other helpful clues are: characteristic skin lesions, elevation of the serum angiotensin-converting enzyme, and a typical gallium scan. Unfortunately, it is extremely difficult to differentiate a testicular tumor from sarcoidosis clinically because a malignant neoplasm of this organ may metastasize to the lungs and hilar lymph nodes and simulate sarcoidosis. Tumor cells may pick up gallium in the scan. Even when a biopsy is done, care must be taken not to depend on the microscopic picture shown by regional nodes because noncaseating granulomas may be found in them if they are in close proximity to a carcinoma.[19] For this reason, it is important that tissue from the testis itself be obtained, and that a biopsy of one of the traditional sarcoidosis organs (lung, mediastinal or cervical nodes) shows a noncaseating granuloma. When these criteria are met, the diagnosis of testicular sarcoidosis can be considered definite.

Should the testicle be biopsied or excised when a mass is found here in a sarcoidosis patient? Chowdhury and associates[8] performed a biopsy in their case, whereas Seaworth et al and other authors[9-12] removed the entire involved testis. Preservation of the testis by biopsy alone appears justified if there is documented sarcoidosis in the usual areas of the body. Currently, it is not known if testicular function is preserved after treatment with prednisone or similar drugs; in any event, it would seem most judicious to save as much of the testis as possible.

Two other features of the case described in this report are that the patient's disease repeatedly relapsed each time he stopped the prednisone and that the testicular mass occurred despite long-term, albeit interrupted, therapy. These facts raise the question of how long steroids should be continued in patients with sarcoidosis. The authors' practice is to treat patients for 6 to 12 months; then review with an eye to discontinue therapy at that time, followed by close observation throughout life. Treatment is restarted if evidence of relapse occurs.

In the authors' experience, repeated relapses of the degree seen in the patient in this report are rare. Johns and associates[20] at Johns Hopkins Hospital treated over 80 percent of their 192 sarcoidosis patients for at least one year. Relapses were recorded in 70 percent of the patients when prednisone was stopped or reduced to less than 10 to 15 mg/day. The specific extent or sites (new or old) are not made clear by the Hopkins group. Their treatment plan was to reduce or discontinue therapy and follow closely for evidence of relapse. The experience with this patient suggests that some individuals with sarcoidosis require therapy for at least 7½ years or perhaps indefinitely as shown by Johns' group,[20] who treated 34 percent of their patients five years or more and 11 percent for over 10 years. Certainly, the case study patient should continue steroids indefinitely.

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